

PCT/US99/20881

SEQUENCE LISTING

<110> Gurney, Mark E.

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Yan, Riqiang

Pharmacia & Upjohn Company

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The authors would like to thank the referees for their constructive comments and suggestions.

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Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr

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Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr

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Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
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Asn Ile Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
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Thr Glu Ala Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
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Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
 260 265 270

Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
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Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
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Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
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Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr

19

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<211> 2088

<212> DNA

<213> Homo sapiens

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Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln
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[illegible]

1. The first step is to identify the key components of the system. This involves understanding the hardware, software, and data involved.

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Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu
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Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
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Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
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Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys
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Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg
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Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp
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Gln Glu Ala Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala
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[illegible]

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 580 585 590
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 595 600 605
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 His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys
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 625 630 635 640
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 645 650 655
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 His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg
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Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp

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Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu

65 70 75 80

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 Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu
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 Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys
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 Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp
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 Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu
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 Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn
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 Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe

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580

585

590

Glu Val Asn Leu Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val

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600

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His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys

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615

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630

635

640

Ile Val Ile Thr Leu Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile

645

650

655

His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg

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35 40 45

Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp

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Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu

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Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val

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Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp
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Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu
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Gln Glu Ala Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala
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Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn
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Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe
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Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His
      420          425          430

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Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala
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 Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu
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 Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala
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 Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn
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 Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser
 500 505 510
 Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr
 515 520 525
 Val Glu Leu Leu Pro Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln
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 Pro Trp His Ser Phe Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn
 545 550 555 560
 Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr
 565 570 575
 Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
 580 585 590
 Glu Val Lys Met Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val

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      595              600              605
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His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys
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Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val
      625              630              635              640
-
-
Ile Phe Ile Thr Leu Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile
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-
His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg
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-
His Leu Ser Lys Met Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys
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Phe Phe Glu Gln Met Gln Asn
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<211> 2094

<212> DNA

<213> Homo sapiens

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Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln
35          40          45
-
Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
50          55          60
-
Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
65          70          75          80
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Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
85          90          95
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Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
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-
Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
115         120         125
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Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Lys
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 Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
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 Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
 180 185 190
 Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
 195 200 205
 Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
 210 215 220
 Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu
 225 230 235 240
 Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
 245 250 255
 Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
 260 265 270
 Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
 275 280 285
 Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu

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Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala
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Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn
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-
Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser
          500          505          510
-
Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr
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Val Glu Leu Leu Pro Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln
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Pro Trp His Ser Phe Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn
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Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr
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-
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
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Glu Val Lys Met Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val
          595          600          605
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His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys
          610          615          620
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Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val
 625 630 635 640

Ile Val Ile Thr Leu Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile
 645 650 655

His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg
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His Leu Ser Lys Met Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys
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Phe Phe Glu Gln Met Gln Asn Lys Lys
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Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln

35 40 45

Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp

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Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu

65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn

85 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val

100 105 110

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu

115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys

130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu

145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
 165 170 175
 Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
 180 185 190
 Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
 195 200 205
 Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
 210 215 220
 Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu
 225 230 235 240
 Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
 245 250 255
 Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
 260 265 270
 Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
 275 280 285
 Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu
 290 295 300
 Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys
 305 310 315 320

Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg
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 Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp
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 Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu
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 Gln Glu Ala Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala
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 Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn
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 Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe
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 -
 Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His
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 Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala
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 Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu
 450 455 460
 -
 Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala
 465 470 475 480
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 Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn

485 490 495
 Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser
 500 505 510
 Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr
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 Val Glu Leu Leu Pro Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln
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 Pro Trp His Ser Phe Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn
 545 550 555 560
 Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr
 565 570 575
 Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
 580 585 590
 Glu Val Asn Leu Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val
 595 600 605
 His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys
 610 615 620
 Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val
 625 630 635 640
 Ile Val Ile Thr Leu Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile
 645 650 655

His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg

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665

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His Leu Ser Lys Met Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys

675

680

685

Phe Phe Glu Gln Met Gln Asn Lys Lys

690

695

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<212> DNA

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Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
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Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
 65 70 75 80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
 85 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
 100 105 110

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
 115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys
 130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
 145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
 165 170 175

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu

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Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
      195      200      205
Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
      210      215      220
Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu
      225      230      235      240
Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
      245      250      255
Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
      260      265      270
Ala Thr Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
      275      280      285
Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu
      290      295      300
Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys
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Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg
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Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp
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-															
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-															
Glu	Val	Glu	Pro	Val	Asp	Ala	Arg	Pro	Ala	Ala	Asp	Arg	Gly	Leu	Thr
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-															
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-															
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-															
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-															
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-															
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-															
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His	Leu	Ser	Lys	Met	Gln	Gln	Asn	Gly	Tyr	Glu	Asn	Pro	Thr	Tyr	Lys

[illegible]

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      690              695
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<211> 446

<212> PRT

<213> Homo sapiens

<400> 22

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Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly

35 40 45

Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser

50 55 60

Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr

65 70 75 80

Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala

85 90 95

Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser

100 105 110

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435

440

445

<210> 23

<211> 1380

<212> DNA

<213> Homo sapiens

<400> 23

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 ggcagagata acttgcagtg ggtgctgccc ccccccctt tctgcatcg ctactaccag 360
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 <211> 459
 <212> PRT
 <213> Homo sapiens

<400> 24
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 35 40 45
 Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly
 50 55 60
 Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly
 65 70 75 80
 Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile
 85 90 95
 Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His
 100 105 110
 Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg
 115 120 125

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-
Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu
130      135      140
-
Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val
145      150      155      160
-
Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe
165      170      175
-
Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu
180      185      190
-
Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val
195      200      205
-
Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu His Leu Cys Gly Ala
210      215      220
-
Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser
225      230      235      240
-
Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp
245      250      255
-
Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg
260      265      270
-
Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn
275      280      285
-

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Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro
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 Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser
 305 310 315 320
 Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys
 325 330 335
 Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu
 340 345 350
 Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu
 355 360 365
 Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp
 370 375 380
 Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met
 385 390 395 400
 Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg
 405 410 415
 Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe
 420 425 430
 Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp
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 Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser

455

<213> Homo sapiens

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<211> 433

<212> PRT

<213> Homo sapiens

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20 25 30

Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg

35 40 45

Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro

50 55 60

Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala

65 70 75 80

Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln

85 90 95

Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr

100 105 110

Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile

115 120 125

Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr
 130 135 140
 Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu
 145 150 155 160
 Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro
 165 170 175
 Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser
 180 185 190
 Leu His Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu
 195 200 205
 Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu
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 Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr
 225 230 235 240
 Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met
 245 250 255
 Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr
 260 265 270
 Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser
 275 280 285
 Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu

290 295 300
 Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile
 305 310 315 320
 Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser
 325 330 335
 Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp
 340 345 350
 Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser
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 Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val
 370 375 380
 Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys
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<211> 1278

<212> DNA

<213> Homo sapiens

<400> 27

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<210> 28

<211> 425

<212> PRT

<213> Homo sapiens

<400> 28

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Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr
           35           40           45

Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val
           50           55           60

Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe
65           70           75           80

Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu
           85           90           95

Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu
           100          105          110

Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val
           115          120          125

Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn
           130          135          140

Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala

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145 150 155 160
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 Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln
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 -
 Thr His Val Pro Asn Leu Phe Ser Leu His Leu Cys Gly Ala Gly Phe
 180 185 190
 -
 Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile
 195 200 205
 -
 Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr
 210 215 220
 -
 Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu
 225 230 235 240
 -
 Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp
 245 250 255
 -
 Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys
 260 265 270
 -
 Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu
 275 280 285
 -
 Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln
 290 295 300
 -
 Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu
 305 310 315 320

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-
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-           325           330           335
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-
Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys
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-           340           345           350
-
-
Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala
-
-           355           360           365
-
-
Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg
-
-           370           375           380
-
-
Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr
-
-           385           390           395           400
-
-
Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly
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-           405           410           415
-
-
Tyr Asn Ile Pro Gln Thr Asp Glu Ser
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-           420           425
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<212> DNA
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<213> Homo sapiens
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<400> 29
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<211> 453

<212> PRT

<213> Homo sapiens

<400> 30

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1

5

10

15

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 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
 35 40 45
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
 50 55 60
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65 70 75 80
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
 85 90 95
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
 100 105 110
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
 115 120 125
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
 130 135 140
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
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 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
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 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp

180 185 190
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
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 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
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 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
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 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
 245 250 255
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
 260 265 270
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 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
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 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
 325 330 335
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 340 345 350

Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg

355 360 365

Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala

370 375 380

Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu

385 390 395 400

Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala

405 410 415

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Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro

435 440 445

Gln Thr Asp Glu Ser

450

<210> 31

<211> 1380

<212> DNA

<213> Homo sapiens

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10

15

Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
 20 25 30
 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
 35 40 45
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
 50 55 60
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65 70 75 80
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
 85 90 95
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
 100 105 110
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
 115 120 125
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
 130 135 140
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
 145 150 155 160
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
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 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp

180 185 190
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
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 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
 210 215 220
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
 225 230 235 240
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
 245 250 255
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
 260 265 270
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
 275 280 285
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
 290 295 300
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
 305 310 315 320
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
 325 330 335
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
 340 345 350

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-
Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
-
355 360 365
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Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
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370 375 380
-
Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
-
385 390 395 400
-
Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
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405 410 415
-
Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
-
420 425 430
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Gln Thr Asp Glu Ser His His His His His His
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-
Ser Ser Leu Val Arg His Arg Trp Lys

20 25

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<213> Homo sapiens

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Ser Glu Gln Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp Ile Ser

1 5 10 15

-
Leu Leu Lys

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<400> 36

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36

<210> 37

<211> 39

<212> DNA

<213> Homo sapiens

<400> 37

gacgatgac tatctctgac tctccgctg aacaggacg

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<210> 38

<211> 39

<212> DNA

<213> Homo sapiens

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<210> 39

<211> 77

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Hu Asp2

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 <223> Description of Artificial Sequence: Hu-Asp2

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 <223> Description of Artificial Sequence: Caspase 8
 Cleavage Site

<400> 41
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<210> 42
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 <212> DNA
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 <223> Description of Artificial Sequence: Caspase 8

Cleavage Site

<400> 42

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<210> 43

<211> 32

<212> DNA

<213> Homo sapiens

<400> 43

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<210> 44

<211> 36

<212> DNA

<213> Homo sapiens

<400> 44

gaaagcttcc atgactcacc tctctgtgga atgttg 36

<210> 45

<211> 24

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: 6-His tag

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-
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-
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 <223> Description of Artificial Sequence: Introduce KK
 motif

-
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 csnayrsnay rh0dtgactg accactcgac caggttcact snayrtccsn asnanrmdt 180
 csnayrtcna mcrtwid0t dtbharmaca hngactgacc actcgaccag gttcttdgda 240
 n0bd0cda00 a0ca0rtntn ygtabwrddc mntemmaryn rmatndcmnt emmarynma 300
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 <210> 48
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 <211> 462

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Introduce KK motif

<403> 48

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_mbarahr0cg aattaaattc sagcacactg gctacttctt gttctgcate tcaaagaacs 180
_nayrsnayrnn 0htagaatta aattncagca cactgggtac ttcttgttct gcattctcaa 240
_gaacgaasna yrttcnashn animadtcn ayrtcnamer stwardcgks kdrharmaca 300
_hnagaattaa attccagcac actgggtact tcttgttctg catctcaag aacttdgdan 360
_0b0cda00a0 ca0rtntryh kktabwrddc mntsmmaryn rnatndcmnt smmaryn.rma 420
_tntdcmbboc tckkcrstw rddcmntsw rddcwrdcm nt 482

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<210> 49

<221> 380

<212> DNA

<213> Artificial Sequence

<220>

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<223> Description of Artificial Sequence:  Introduce KK
      mo-if

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<400> 49

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cactggctas	nayrsnayrh	ddhcggaatta	aattccagca	cactggctag	aas:ayrttc	180
snasnarma	dtcsnayrtc	namcrstwr	cmndhharma	cahncgaatt	aaattccagc	240

[illegible]

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PCT/US99/20881

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_dmmntmswr0 dcvrddcmnt 380
-
-

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